REMARKS

I. Disposition of the Claims

Claims 1-40 and 48-51 are pending. Claims 44-47 have been cancelled without prejudice or disclaimer. Claims 48-51 are new, and like claims 44-47, should be withdrawn and should be rejoined once claims 1, 11, 21, and 31, respectively, have been allowed. Claims 2, 5-12, 14-20, 22, 25-32, and 34-40 have been rejected. Claims 1, 3-4, 21, 23-24, and 34 have been allowed. Office action, para. 7. Claims 13 and 33 are objected to for depending on a rejected base claim but are otherwise allowable if rewritten in independent form. Office action, para. 6.

Claims 11, 14, and 31 have been amended as shown. Support is in the specification as-filed.

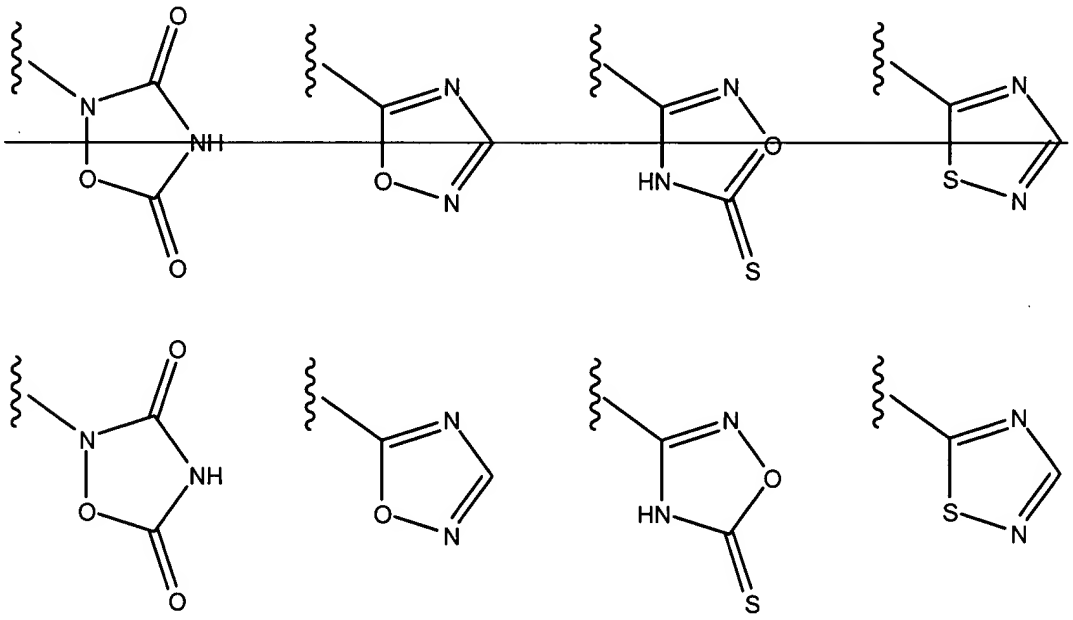
Claims 48-51, respectively, should be rejoined with the elected group when claims 1, 11, 21 and 31, respectively, have been allowed. "Process claims which depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance." MPEP § 821.04. In other words, if a product claim is found allowable, Applicant may add claims directed to the process of making the patentable product. Here, claims 1 and 21 are allowable. Thus, claims 48 and 50 should be rejoined with the elected group as a matter of right. Additionally, claims 49 and 51 are believed allowable and should be rejoined as a matter of right.

The PTO is thanked for indicating allowable subject matter. Office action, para. 4.

II. Comments about the Amendment of January 24, 2003.

Applicants' representative inadvertently introduced a change into claims 1, 4, 7, 11 and 14, but did not indicate the change in the version with markings to show changes

made. The change is in the definition of R_1's heterocycles (third one over, third one down) shown here:



Notice the third chemical formula has a double bond between the S=C=O in the strike out version but a single bond between the S=C-O in the corrected version. Applicants' representative noticed this error when preparing the amendment to claim 31 of the present paper.

It is submitted that this error and its solution would have been obvious to one of ordinary skill in the art when the specification was filed. Thus, no new matter has been added by this correction.

The PTO should expect a Supplemental Amendment to correct claims 17, 21, 24, 27, 31, 34, and 37. If the PTO must examine this application but does not have the Supplemental Amendment in the file, please contact Sean A. Passino (45,943), who will assure that the PTO gets a copy of the as-filed paper from its file.

III. Objection to the Specification

The specification has been objected to because "''pyrazinecarboxylate' ... is inconsistent with the formula when n equals 1." Office action, pp. 2-3. This amendment adds the text of claims 3 and 13 in the appropriate location of the specification. No new matter has been added. Thus, this objection should be withdrawn.

IV. Rejections under 35 USC § 102

Various claims have been rejected as anticipated by the disclosures of Kobayashi (EP 0 104,484) and Delaszlo (US Pat. No. 6,069,163). Each rejection is addressed under a separate subheading.

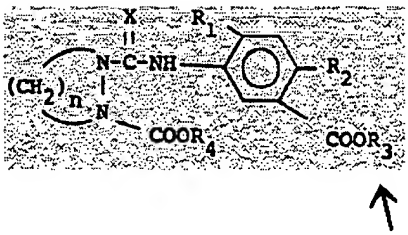
A. Kobayashi

Claim 31 stands rejected over Kobayashi. Office action , para. 1. The comments about the "ester thereof" are acknowledged and appreciated.

Yet Kobayashi never describes or anticipates a compound of claim 31. Kobayashi contains the following cited disclosure:

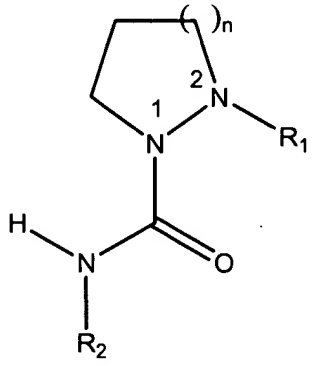
Table 2

Compound No.	n	X	R_1	R_2	R_3	R_4
39	3	O	F	Cl	CH_3	C_2H_5
40	3	O	F	Cl	C_2H_5	"
41	3	O	F	Cl	C_3H_7 (i)	"



Kobayashi, pp. 17-18. Note particularly that the aromatic $-COOR_3$ group (lower-right-hand side) is a specified ester.

On the other hand, claim 31 recites a compound of formula IV:



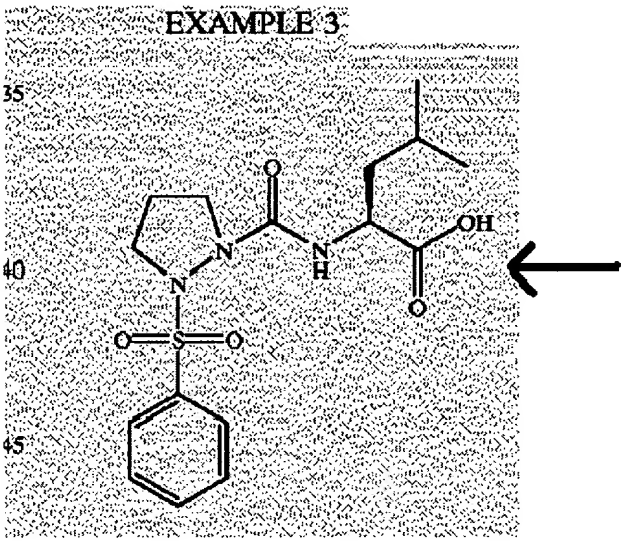
IV

in which R_2 may be an aryl substituted with one or more substituents selected from those other than Kobayashi's ester groups.

As a result, since the presently claimed R_2-aryl substituents cannot be selected from Kobayashi's ester groups, and since the Kobayashi's cited-aromatic $-COOR_3$ groups are particular esters, the presently claimed compounds differ from those of Kobayashi. In other words, Kobayashi neither describes nor anticipates the compound of claim 31. Thus, this rejection is improper and should be withdrawn.

B. Delaszlo

Claims 11 and 14 stand rejected as anticipated by Delaszlo's compound 3:



Office action, p. 5. Note particularly the Examiner's proposed amendment has been adopted, i.e., deleting "carboxy" from the list of R_3's substituents. Additionally, the term "carboxy" was returned to the list of R_3's members.

As neither claim 11 nor 14 embraces Delaszlo's compound 3, Delaszlo neither describes nor anticipates claim 11 or 14. Thus, this rejection is improper and should be withdrawn.

V. Rejections under 35 USC § 112, first paragraph

Three sets of claims are rejected for lack of enablement. Each rejection is addressed under a separate heading.

A. Claims 7-10, 17-20, 27-30, and 37-40

Claims 7-10, 17-20, 27-30, and 37-40 are rejected because, although the specification is enabling "for the method of treating Parkinson's disease," it is not enabling

"for the method of treating Alzheimer's disease, Huntington's disease, and other neuronal activity (e.g., promoting neuronal regeneration, preventing neurodegeneration, etc.)." Office action, para. 3. This rejection is improper and should be withdrawn.

Claims are assumed enabled. MPEP § 2164.04. Indeed, when challenging a claim's enablement, the PTO must not only explain why it doubts the claim's presumptively enabling disclosure but also cite supporting evidence for its assertion. Id. Indeed, the PTO never cited sufficient evidence to support its assertions, even though all factual findings that are material to patentability must be supported by substantial evidence. In re Zurko, 258 F.3d 1379, 1386 (Fed. Cir. 2001). In this rejection, however, the PTO cited virtually no evidence to support its findings.

Furthermore, the PTO's explanation must further include specific technical reasons that cast doubt on the claim's enablement. Id. Yet, in the present rejection, the PTO's explanation consists of mere conclusions.

As neither evidence nor explanation of record casts doubts on the present claim's enablement, the rejection is improper and should be withdrawn.

B. Claims 7, 17, 27, and 37

Claims 7, 17, 27, and 37 have been rejected. Office action, para. 3. The PTO makes several findings in the paragraph bridging pages 5-6 of the Office action. With all due respect, the PTO never cited sufficient evidence to support its assertions, even though all factual findings that are material to patentability must be supported by substantial evidence. Zurko, 258 F.3d at 1386. Thus, the rejection is improper and should be withdrawn.

If the PTO maintains the rejection, the PTO is asked to cite supporting evidence for its findings so that Applicants could evaluate the evidence and formulate an appropriate response.

C. Claims 5-6, 15-16, and 35-36

Claims 5-6, 15-16, and 35-36 have been rejected. Office action, para. 4. According to the PTO, there is a concern about the neurotrophic factor's ability to be "metabolized in the gastrointestinal tract, and liver, and thus will lose efficacy." With all due respect, the PTO never cited sufficient evidence to support its assertions, even though all factual findings that are material to patentability must be supported by substantial evidence. Zurko, 258 F.3d at 1386. Thus, the rejection is improper and should be withdrawn.

Furthermore, the enablement test for compositions should not be limited to a particular form or particular means of administration, such as oral administration. This is especially true when the specification describes various administration routes. Spec. p. 81-et seq. And, according to the evidence and explanation, it is unclear why every administration route would be expected to result in a neurotrophic factor that is "metabolized in the gastrointestinal tract, and liver, and thus will lose efficacy." Thus, the rejection is improper and should be withdrawn, especially since claims are assumed enabled.

VI. Rejections under 35 USC § 112, second paragraph

Claims 2, 12, 22, and 32 have been rejected as indefinite because "the preamble non-immunosuppressive does not result in a structural change." Office action, para. 5. A claim is proper under 35 USC § 112, second paragraph if it reasonably apprises one of ordinary skill in the art of its scope. MPEP § 2173.02. Here, e.g., claim 2 reads "The compound of claim 1, wherein the compound is non-immunosuppressive." Thus, merely reading claims 1-2 suggests that some compounds of claim 1 are immunosuppressive and some are non-immunosuppressive and that the compounds of claim 2 are chosen from the non-immunosuppressive compounds of claim 1.

Along these lines, the present specification states "A preferred feature of the compounds of the present invention is that they do not exert any significant immunosuppressive activity and/or are non-immunosuppressive." Spec. p. 18, ll. 4-7. In other words, some compounds are immunosuppressive and some are non-immunosuppressive. Thus, merely reading this passage and claims 1-2 provides evidence which tends to support that one of ordinary skill in the art would have been reasonably apprised of claim 2's scope.

A similar analysis may be made for the other claims. Therefore, this rejection is improper and should be withdrawn.

CONCLUSION

Applicants respectfully request reconsideration and reexamination of the present application. Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

Respectfully submitted,

Date 7/14/3

By _____

FOLEY & LARDNER
Customer Number: 29728
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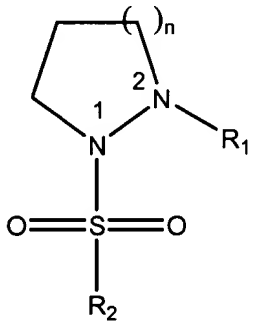
Sean A. Passino
Attorney for Applicants
Registration No. 45,943

Version With Markings to Show Changes Made

In the Claims:

11. (Twice Amended) A compound of formula II:

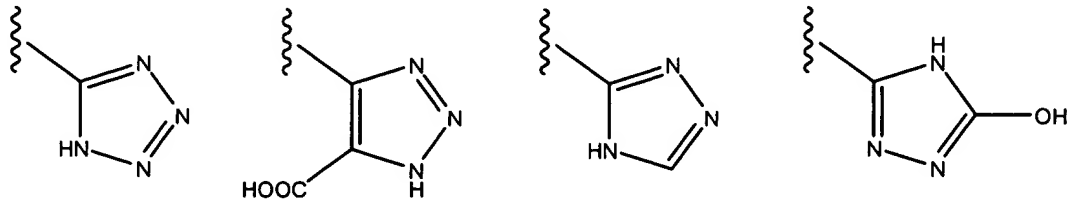


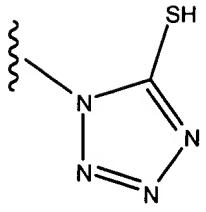
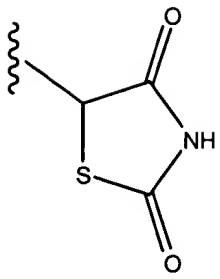
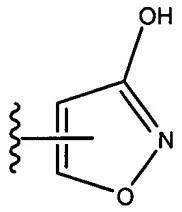
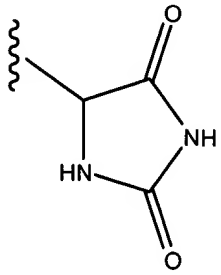
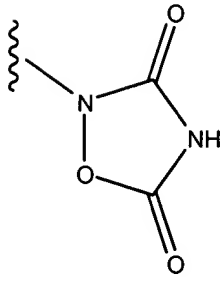
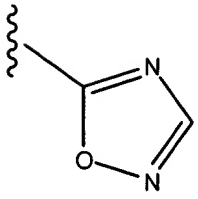
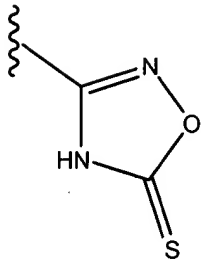
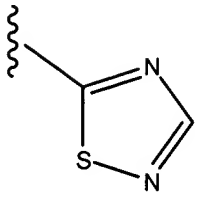
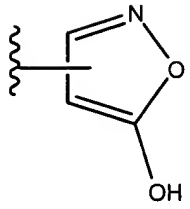
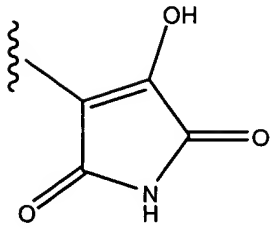
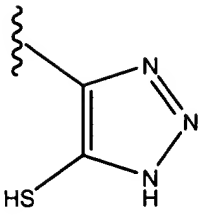
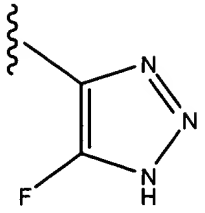
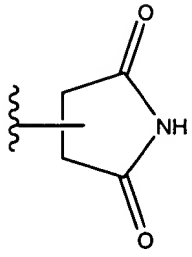
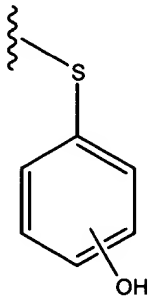
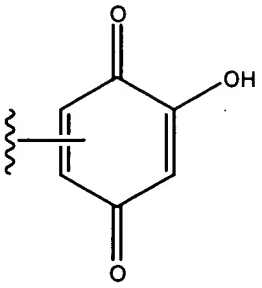
II

or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n = 1-3;

R_1 is selected from the group consisting of $-CR_3$, $-COOR_3$, $-COR_3$, $-COOH$, $-SO_3H$, $-SO_2HNR_3$, $-PO_2(R_3)_2$, $-CN$, $-PO_3(R_3)_2$, $-OR_3$, $-SR_3$, $-NHCOR_3$, $-N(R_3)_2$, $-CON(R_3)_2$, $-CONH(O)R_3$, $-CONHNHSO_2R_3$, $-COHNSO_2R_3$, $-CONR_3CN$,



wherein said R_1 group is either unsubstituted or additionally substituted with R_3;

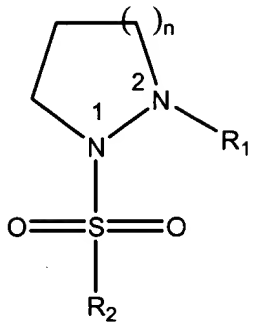
R_2 is selected from the group consisting of hydrogen, C_1-C_9 straight or branched chain alkyl, C_2-C_9 straight or branched chain alkenyl, C_2-C_9 straight or branched chain alkynyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, alkynyl, aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted or substituted with one or more substituents selected from R_3;

R_3 is selected from the group consisting of hydrogen, C_1-C_9 alkyl, C_2-C_9 straight or branched chain alkenyl, C_2-C_9 straight or branched chain alkynyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, **carboxy,** C_1-C_9 thioalkyl, C_2-C_9 thioalkenyl, C_1-C_9 alkylamino, C_2-C_9 alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, **[carboxy,]** carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocyle, or heterocycle group.

14. (Amended) A pharmaceutical composition comprising:

(i) a therapeutically effective amount of a compound of formula II:

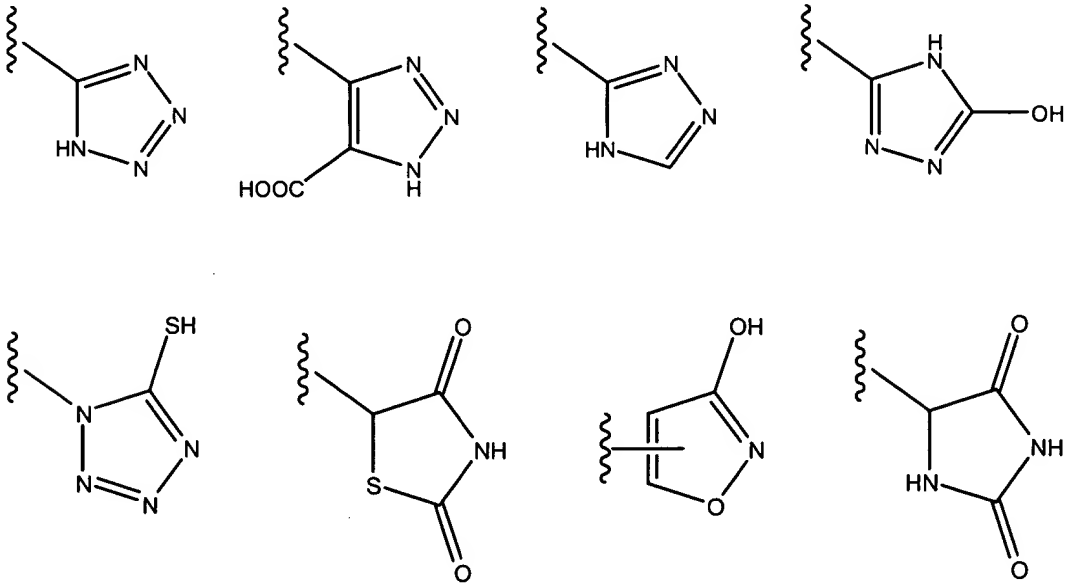


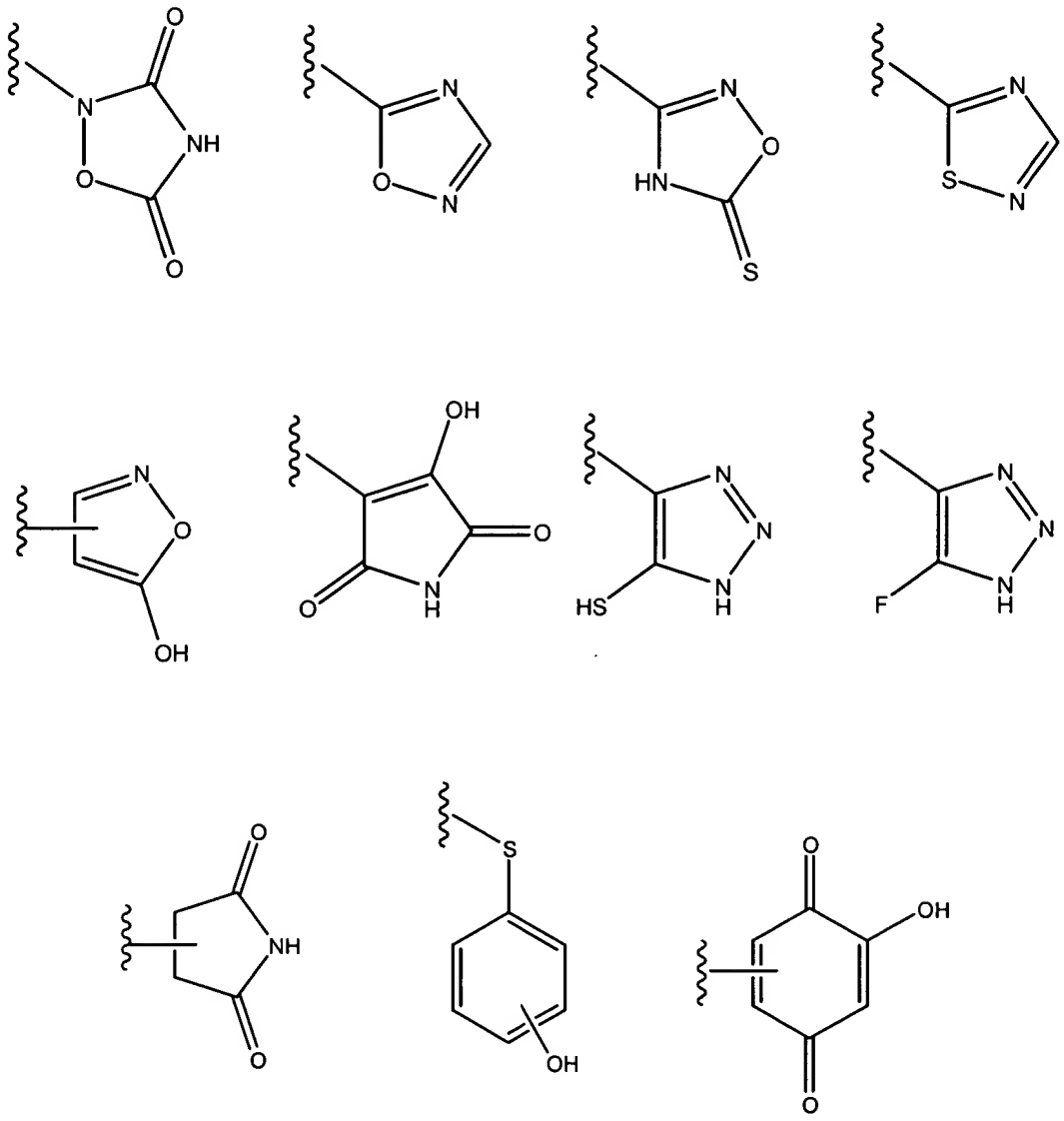
II

or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n = 1-3;

R_1 is selected from the group consisting of $-CR_3$, $-COOR_3$, $-COR_3$, -COOH, $-SO_3H$, $-SO_2HNR_3$, $-PO_2(R_3)_2$, -CN, $-PO_3(R_3)_2$, $-OR_3$, $-SR_3$, $-NHCOR_3$, $-N(R_3)_2$, $-CON(R_3)_2$, $-CONH(O)R_3$, $-CONHNHSO_2R_3$, $-COHNSO_2R_3$, $-CONR_3CN$,





wherein said R_1 group is either unsubstituted or additionally substituted with R_3;

R_2 is selected from the group consisting of hydrogen, C_1-C_9 straight or branched chain alkyl, C_2-C_9 straight or branched chain alkenyl, C_2-C_9 straight or branched chain alkynyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, alkynyl,

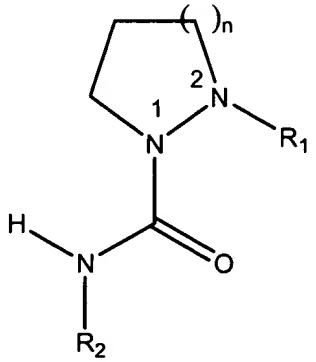
aryl, heteroaryl, carbocycle, or heterocycle is unsubstituted or substituted with one or more substituents selected from R_3;

R_3 is selected from the group consisting of hydrogen, C_1-C_9 alkyl, C_2-C_9 straight or branched chain alkenyl, C_2-C_9 straight or branched chain alkynyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, **carboxy,** C_1-C_9 thioalkyl, C_2-C_9 thioalkenyl, C_1-C_9 alkylamino, C_2-C_9 alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, **[carboxy,]** carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocyle, or heterocycle group; and

(ii) a pharmaceutically acceptable carrier.

31. (Amended) A compound of formula IV:

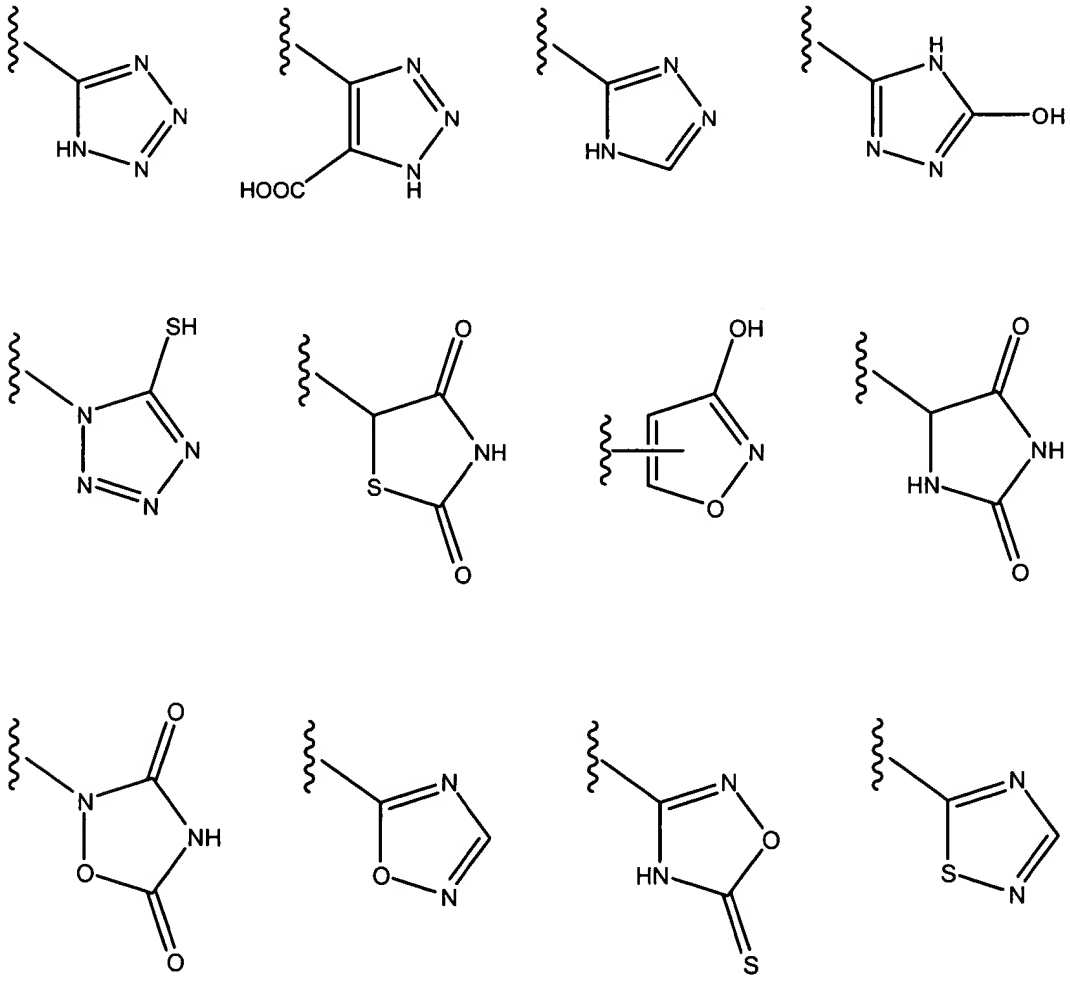


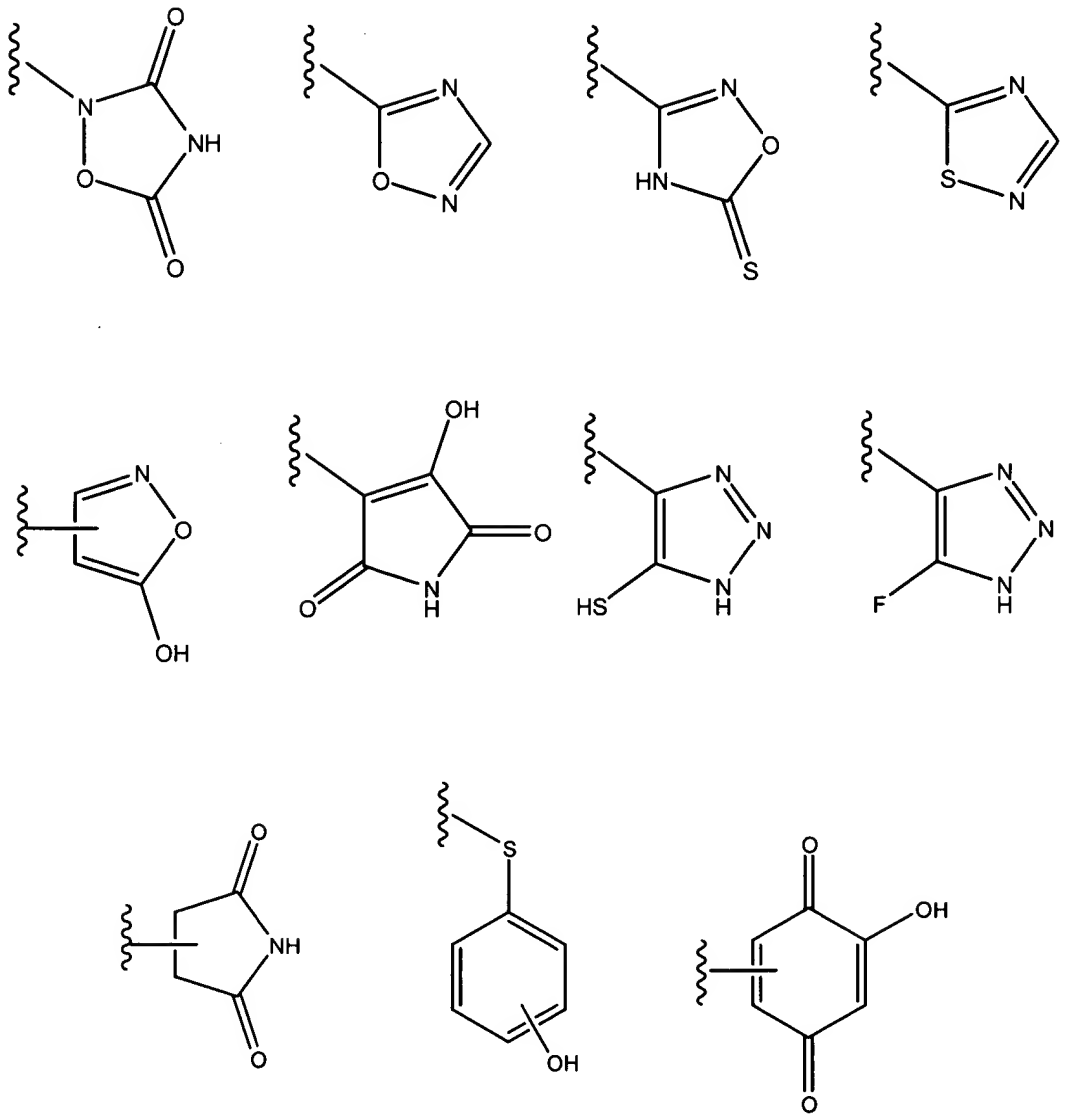
IV

or a pharmaceutically acceptable salt, ester or solvate thereof, wherein:

n is 1-3;

R_1 is selected from the group consisting of $-CR_3$, $-COOR_3$, $-COR_3$, -COOH, $-SO_3H$, $-SO_2HNR_3$, $-PO_2(R_3)_2$, -CN, $-PO_3(R_3)_2$, $-OR_3$, $-SR_3$, $-NHCOR_3$, $-N(R_3)_2$, $-CON(R_3)_2$, $-CONH(O)R_3$, $-CONHNHSO_2R_3$, $-COHNSO_2R_3$, $-CONR_3CN$,





wherein said R_1 group is either unsubstituted or additionally substituted with R_3; and

R_2 is C_1-C_9 alkyl, C_2-C_9 alkenyl, aryl, heteroaryl, carbocycle, or heterocycle, wherein said alkyl, alkenyl, aryl, heteroaryl, carbocycle, or heterocycle is substituted with one or more substituent(s) selected from R_3; and

R_3 is selected from the group consisting of hydrogen, C_1-C_9 alkyl, C_2-C_9 straight or branched chain alkenyl, C_2-C_9 straight or branched chain alkynyl, C_1-C_9 alkoxy, C_2-C_9 alkenyloxy, aryloxy, phenoxy, benzyloxy, hydroxy, carboxy, C_1-C_9 thioalkyl, C_2-C_9 thioalkenyl, C_1-C_9 alkylamino, C_2-C_9 alkenylamino, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocycle, and heterocycle,

wherein said alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, aryloxy, thioalkyl, thioalkenyl, alkylamino, alkenylamino, aryl, heteroaryl, carbocycle, or heterocycle group is optionally substituted with a hydroxy, **[carboxy,]** carbonyl, cyano, nitro, imino, sulfonyl, thiocarbonyl, sulfhydryl, halo, haloalkyl, trifluoromethyl, aryl, heteroaryl, carbocyle, or heterocycle group.